

Variant: *NM_000038.6(APC):c.1746A>G (p.Glu582=)*

Version: 1.0

CA10578326 [↗](#)

231116 (ClinVar) [↗](#)

Gene: APC ([HGNC:324](#))

Condition: familial adenomatous polyposis 1 ([MONDO:0021056](#))

Inheritance Mode: Autosomal dominant inheritance

UUID: 952838c6-8886-4533-8058-ef40f2af56c4

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HGVS expressions

NM_000038.6:c.1746A>G

NM_000038.6(APC):c.1746A>G (p.Glu582=)

NC_000005.10:g.112834953A>G

CM000667.2:g.112834953A>G

NC_000005.9:g.112170650A>G

CM000667.1:g.112170650A>G

NC_000005.8:g.112198549A>G

NG_008481.4:g.147433A>G

ENST00000502371.3:c.1411A>G

ENST00000504915.3:c.1800A>G

ENST00000505350.2:c.*1752A>G

ENST00000507379.6:c.1692A>G

ENST00000509732.6:c.1746A>G

ENST00000512211.7:c.1746A>G

ENST00000257430.9:c.1746A>G

ENST00000257430.8:c.1746A>G

ENST00000502371.2:c.99A>G

ENST00000504915.2:c.435A>G

ENST00000507379.5:c.1692A>G

ENST00000508376.6:c.1746A>G

ENST00000508624.5:c.*1068A>G

ENST00000512211.6:c.1746A>G

ENST00000520401.1:c.230+5981A>G

NM_000038.5:c.1746A>G

NM_001127510.2:c.1746A>G

NM_001127511.2:c.1692A>G

NM_001354895.1:c.1746A>G

NM_001354896.1:c.1800A>G

NM_001354897.1:c.1776A>G

NM_001354898.1:c.1671A>G

NM_001354899.1:c.1662A>G

NM_001354900.1:c.1623A>G

NM_001354901.1:c.1569A>G

NM_001354902.1:c.1473A>G

NM_001354903.1:c.1443A>G

NM_001354904.1:c.1368A>G

NM_001354905.1:c.1266A>G

NM_001354906.1:c.897A>G
NM_001127510.3:c.1746A>G
NM_001127511.3:c.1692A>G
NM_001354895.2:c.1746A>G
NM_001354896.2:c.1800A>G
NM_001354897.2:c.1776A>G
NM_001354898.2:c.1671A>G
NM_001354899.2:c.1662A>G
NM_001354900.2:c.1623A>G
NM_001354901.2:c.1569A>G
NM_001354902.2:c.1473A>G
NM_001354903.2:c.1443A>G
NM_001354904.2:c.1368A>G
NM_001354905.2:c.1266A>G
NM_001354906.2:c.897A>G

Benign

Met criteria codes 4

BS1 BS2 BP7 BP4

Evidence Links 0

Expert Panel

InSiGHT Hereditary Colorectal Cancer/Polypsis VCEP

Criteria Specification Information

Criteria Specifications for this VCEP

Evidence submitted by expert panel

InSiGHT Hereditary Colorectal Cancer/Polypsis VCEP

The c.1746A>G (p.Glu582=) variant in APC is a synonymous (silent) variant that is not predicted to impact splicing (BP4, BP7). This variant has been observed in a heterozygous state in 12 unrelated healthy adult individuals worth 12 (≥ 10) healthy individual points in total (BS2; Ambry internal data). The highest population minor allele frequency of this variant in gnomAD v2.1.1 (non-cancer) is 0.0001148 in African/African American population, which is higher than the ClinGen InSiGHT Hereditary Colorectal Cancer/Polypsis threshold (≥ 0.0001) for BS1, and therefore meets this criterion (BS1). In summary, this variant meets the criteria to be classified as Benign for FAP based on the ACMG/AMP criteria applied, as specified by the ClinGen InSiGHT Hereditary Colorectal Cancer/Polypsis Variant Curation Expert Panel: BS1, BS2, BP4, and BP7 (VCEP specifications version 1; date of approval: 12/12/2022).

Met criteria codes

BS1



The highest population minor allele frequency of the variant c.1746A>G in gnomAD v2.1.1 (non-cancer) is 0.0001148 (1/8712 alleles) in African/African American population, which is higher than the ClinGen InSiGHT Hereditary Colorectal Cancer/Polypsis threshold threshold (≥ 0.0001) for BS1, and therefore meets this criterion (BS1).

BS2



This variant has been observed in heterozygous state in 12 healthy unrelated adult individuals worth 12 (≥ 10) healthy individual points in total (BS2; Ambry internal data).

BP7



The c.1746A>G (p.Glu582=) variant is a synonymous (silent) variant that is not predicted by MaxEntScan, SpliceAI and varSEAK to impact splicing (BP4, BP7).

BP4



The results from 3 in silico splicing predictors (MaxEntScan, SpliceAI, varSEAK) support that this variant does not affect splicing (BP4).

Curation History [↗](#)

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